	FILE	'HCAPLUS' ENTERED AT 13:25:03 ON 14 JUN 2007
L1		30329 S LYSOZYME OR MURAMIDASE
L2		21350 S SIRS OR (SYSTEMIC INFLAMMATORY RESPONSE) OR SEPSIS OR ((SEPTI
L3		1362 S (MYOCARDIAL(W) (DYSFUNCTION OR DEPRESSION))
L4.		49845 S (CHITOBIOSE OR CHITOTRIOSE OR CHITIN OR CHITOSAN OR (N-ACETYL
L5 ·		57 S L1 AND L2
L6		4 S L1 AND L2 AND L3
L7		6 S L1 AND L2 AND L4
L8		2 S L1 AND L2 AND L3 AND L4
	FILE	'HCAPLUS' ENTERED AT 13:46:53 ON 14 JUN 2007
L9		1118 S (LYSOZYME OR MURAMIDASE) (3A) (INHIBI?)
L10		7 S L2 AND L9
L11		5 S L10 AND (PY<2004 OR AY<2004 OR PRY<2004)
	FILE	'REGISTRY' ENTERED AT 14:20:18 ON 14 JUN 2007
L12		1 S KETOROLAC/CN
	FILE	'CAPLUS' ENTERED AT 14:20:47 ON 14 JUN 2007
L13		773 S L12/THU
L14		7 S L13 AND L2

=> file hcaplus
COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 0.84 0.84

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FILE COVERS 1907 - 14 Jun 2007 VOL 146 ISS 25 FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s lysozyme or muramidase

29907 LYSOZYME

1204 MURAMIDASE

L1 30329 LYSOZYME OR MURAMIDASE

=> s SIRS or (systemic inflammatory response) or sepsis or ((septic or toxic)(w)shock)

890 SIRS

103641 SYSTEMIC

180565 INFLAMMATORY

1596202 RESPONSE

1915 SYSTEMIC INFLAMMATORY RESPONSE

(SYSTEMIC (W) INFLAMMATORY (W) RESPONSE)

15541 SEPSIS

13609 SEPTIC

254096 TOXIC

146275 SHOCK

6500 (SEPTIC OR TOXIC) (W) SHOCK

L2 21350 SIRS OR (SYSTEMIC INFLAMMATORY RESPONSE) OR SEPSIS OR ((SEPTIC OR TOXIC) (W) SHOCK)

=> s (myocardial(w)(dysfunction or depression))

68704 MYOCARDIAL

54871 DYSFUNCTION

82704 DEPRESSION

L3 1362 (MYOCARDIAL (W) (DYSFUNCTION OR DEPRESSION))

=> s (chitobiose or chitotriose or chitin or chitosan or (N-acetylglucosamine))

664 CHITOBIOSE

284 CHITOTRIOSE

16498 CHITIN

27636 CHITOSAN

3048197 N

12616 ACETYLGLUCOSAMINE

11365 N-ACETYLGLUCOSAMINE

(N(W) ACETYLGLUCOSAMINE)

L4 49845 (CHITOBIOSE OR CHITOTRIOSE OR CHITIN OR CHITOSAN OR (N-ACETYLGLU COSAMINE))

=> s l1 and l2

L5 57 L1 AND L2

=> s 11 and 12 and 13

L6 4 L1 AND L2 AND L3

=> s 11 and 12 and 14

L7 6 L1 AND L2 AND L4

=> s 11 and 12 and 13 and 14

L8 2 L1 AND L2 AND L3 AND L4

=> file stnguide

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 2.60 3.44

FULL ESTIMATED COST

FILE 'STNGUIDE' ENTERED AT 13:25:11 ON 14 JUN 2007 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jun 8, 2007 (20070608/UP).

=> d l6 1-4 ti abs bib YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L6 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Lysozyme binding to endocardial endothelium mediates myocardial depression by the nitric oxide guanosine 3',5' monophosphate pathway in sepsis

AB Inflammatory mediators have been implicated as a cause of reversible myocardial depression in septic shock

. We previously reported that the release of lysozyme-c (Lmz-S) from leukocytes from the spleen or other organs contributes to myocardial dysfunction in Escherichia coli septic shock in dogs by binding to a cardiac membrane glycoprotein. However, the mechanism by which Lzm-S causes this depression has not been elucidated. In the present study, we tested the hypothesis that the binding of Lzm-S to a membrane glycoprotein causes myocardial depression by the formation of nitric oxide (NO). NO generation then activates soluble guanylyl cyclase and increases cGMP (cGMP), which in turn triggers contractile impairment via activation of cGMP-dependent protein kinase (PKG). We examined these possibilities in a right ventricular trabecular preparation in which isometric contraction was used to measure cardiac contractility. We found that Lzm-S's depressant effect could be prevented by the non-specific NO synthase (NOS) inhibitor NG-monomethyl-L-arginine (L-NMMA). A guanylyl cyclase inhibitor (ODQ) and a PKG inhibitor (Rp-8-Br-cGMP) also attenuated Lzm-S's depressant effect

as did chemical denudation of the endocardial endothelium (EE) with Triton X-100 (0.5%). In EE tissue, we further showed that Lzm-S caused NO release with use of 4,5 diamino-fluorescein, a fluorescent dye that binds to NO. The present study shows that the binding of Lzm-S to EE generates NO, and that NO then activates the myocardial guanosine 3',5' monophosphate pathway leading to cardiac depression in sepsis.

AN 2005:1034020 HCAPLUS <<LOGINID::20070614>>

DN 143:475899

- TI Lysozyme binding to endocardial endothelium mediates myocardial depression by the nitric oxide guanosine 3',5' monophosphate pathway in sepsis
- AU Mink, Steven N.; Bose, Ratna; Roberts, Diane E.; Jacobs, Hans; Duke, Krika; Bose, Deepak; Cheng, Zhao-Qin; Light, R. Bruce
- CS Departments of Medicine and Pharmacology and Therapeutics, Health Sciences Center, University of Manitoba, Winnipeg, MB, R3E-0Z3, Can.
- SO Journal of Molecular and Cellular Cardiology (2005), 39(4), 615-625 CODEN: JMCDAY; ISSN: 0022-2828
 - PB Elsevier B.V.
 - DT Journal
 - LA English
 - RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
 - L6 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
 - TI Methods of treating inflammation
 - AB Methods and compns. for treating myocardial dysfunction or inflammation are described. The methods of the invention involve administering an agent that can inhibit lysozyme to an animal in need thereof. Preferred lysozyme inhibitors include TAC (N,N',N"-triacetylglucosamine, chitotriose) and chitobiose.
 - AN 2004:905606 HCAPLUS <<LOGINID::20070614>>
 - DN 141:360677
 - TI Methods of treating inflammation
 - IN Mink, Steven N.; Jacobs, Hans; Bose, Deepak; Duke, Krika; Light, R. Bruce
 - PA Can
 - SO U.S. Pat. Appl. Publ., 70 pp. CODEN: USXXCO
 - CODEN. OB
 - DT Patent
 - LA English
 - FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
ΡI	US 2004214792	A1	20041028	US 2004-762581	20040123		
	CA 2428744	A1	20040724	CA 2003-2428744	20030512		
PRAI	US 2003-442060P	P	20030124				

- L6 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI N,N',N"-triacetylglucosamine, an inhibitor of lysozyme, prevents myocardial depression in Escherichia coli sepsis in dogs
- AB OBJECTIVE: Reversible myocardial depression in sepsis has been ascribed to the release of inflammatory mediators. We recently found that lysozyme c (Lzm-S), consistent with that originating from the spleen, was a mediator of myocardial depression in an Escherichia coli model of septic shock in dogs. We further showed in a right ventricular trabecular (RVT) preparation that Lzm-S's depressant activity could be blocked by N,N',N" triacetylglucosamine (TAC), a competitive inhibitor of Lzm-S. We hypothesized that Lzm-S binds to or cleaves a cardiac membrane glycoprotein, thereby interfering with myocardial contraction in sepsis. In the present study, we examined whether TAC could prevent myocardial depression in an in vivo preparation and whether other related N-acetylglucosamine (NAG) structures could also inhibit Lzm-S's effect in RVT. DESIGN: Randomized exptl. study. SETTING:

University laboratory SUBJECTS: Anesthetized, mech. ventilated dogs. INTERVENTIONS: We produced sepsis by infusion of E. coli over an approx. 6-h period. MEASUREMENTS AND MAIN RESULTS: We examined the effect of TAC on stroke work, our primary index of myocardial function, when treatment was administered before sepsis (pretreatment) and after 1.5 h (early treatment study) and 3.5 h of sepsis (late treatment study; LTS). In the pretreatment study and early treatment study, myocardial depression would have not yet occurred but would have already been present in the late treatment study. In RVT, we assessed the effect of other NAG oligosaccharides and variants to the NAG structure on Lzm-S's depressant activity. In pretreatment and the early treatment study, TAC prevented the reduction in stroke work observed

in

nontreated septic groups but did not reverse the reduction found in the late treatment study. In RVT, of the compds. tested, only N,N'-diacetylglucosamine showed an inhibitory effect. CONCLUSIONS: We found that TAC, a competitive inhibitor of Lzm-S, prevented myocardial depression in exptl. sepsis. Only specific NAG structures are inhibitory to Lzm-S's depressant activity. TAC may be useful in attenuating cardiovascular collapse in sepsis.

AN 2004:10964 HCAPLUS <<LOGINID::20070614>>

DN 141:133790

TI N,N',N"-triacetylglucosamine, an inhibitor of lysozyme, prevents myocardial depression in Escherichia coli sepsis

AU Mink, Steven N.; Jacobs, Hans; Duke, Krika; Bose, Deepak, Cheng, Zhao-Qin, Light, R. Bruce

CS Departments of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, MB, R3E 0Z3, Can.

SO Critical Care Medicine (2004), 32(1), 184-193

CODEN: CCMDC7; ISSN: 0090-3493

PB Lippincott Williams & Wilkins

DT Journal

LA English

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Lysozyme: a mediator of myocardial depression

and adrenergic dysfunction in septic shock in dogs

AB The objective of the present study was to identify the nature of a filterable cardiodepressant substance (FCS) that contributes to myocardial dysfunction in a canine model of Escherichia coli septic shock. In a previous study, it was found that FCS increased in plasma after 4 h of bacteremia (Am J Physiol 1993;264:H1402) in which FCS was identified by a bioassay that included a right ventricular trabecular (RVT) preparation In that study, FCS was only partially identified by pore filtration techniques and was found to be a protein of mol. weight between 10 and 30 K. In the present study, FCS was further purified by size exclusion high-pressure liquid chromatog., until a single band was identified on one-dimensional gel electrophoresis. band was then subjected to tandem mass spectrometry and protein-sequencing techniques and both techniques identified FCS as lysozyme c (Lzm-S), consistent with that originating from the canine spleen. Confirmatory tests showed that purified Lzm-S produced myocardial depression in the RVT preparation at concns. achieved during sepsis in the in vivo preparation In addition, Lzm-S inhibited the adrenergic response induced by field stimulation and the β - agonist isoproterenol in in vitro prepns., these results suggesting that Lzm-S may inhibit the sympathetic response in sepsis. The present findings indicate that Lzm-S originating from disintegrating leukocytes from organs such as the spleen contributes to myocardial dysfunction in this model. The mechanism may relate to its binding or hydrolysis of a cardiac membrane glycoprotein thereby

interfering with myocardial excitation-contraction coupling in sepsis.

- AN 2003:251561 HCAPLUS <<LOGINID::20070614>>
- DN 139:20409
- TI Lysozyme: a mediator of myocardial depression and adrenergic disfunction in septic shock in dogs
- AU Mink, Steven N.; Jacobs, Hans; Bose, Deepak; Duke, Krika; Cheng, Zhao-Qin; Liu, Gang; Light, R. Bruce
- CS Department of Medicine, University of Manitoba, Winnipeg, MB, R3E-0Z3, Can.
- SO Journal of Molecular and Cellular Cardiology (2003), 35(3), 265-275
 CODEN: JMCDAY; ISSN: 0022-2828
- PB Elsevier Science Ltd.
- DT Journal
- LA English
- RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 17 1-6 ti YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

- L7 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Kinetic analysis of interaction between lipopolysaccharide and biomolecules
- L7 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Analysis of complex gene expression profiles using an analysis of the cellular composition of the sample to identify cell-type-specific signatures
- L7 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of treating inflammation
- L7 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI N,N',N"-triacetylglucosamine, an inhibitor of lysozyme, prevents myocardial depression in Escherichia coli sepsis in dogs
- L7 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Means and methods for detecting endoglycosidase activity
- L7 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Chemical and biological characteristics of human lysozyme isolated from placenta

=> d 17 1 2 5 6 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

- L7 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Kinetic analysis of interaction between lipopolysaccharide and biomolecules
- AB Lipopolysaccharide(LPS) is a major component of the outer membrane of all gram-neg. bacteria. It is a heat-resistant toxin which can cause toxic shock in animals. LPS interacts with some biomols. and triggers its toxic reaction. In this study, the interaction between LPS from Salmonella Minnesota and some biomols. using surface okasnib resibabce (SPR) biosensor. biomols. were imobilized on CM5 sensor-chip suing amion coupling method and LPS was injected over the immobilized surfaces. The affinity consts. kA of LPS with serum albumin,

```
Hb, chitosan and lysozyme were 2.36 \times 107, 2.03 \times 108,
     7.58 x 106, 2.82 x 104 L/mol, resp. But LPS could not interact with
     ferritin.
     2007:624325 HCAPLUS <<LOGINID::20070614>>
AN
ΤI
     Kinetic analysis of interaction between lipopolysaccharide and
     biomolecules
AU
     Yang, Fan; Yang, Xiu-Rong
CS
     State Key Laboratory of Electroanalytical Chemistry, Changchun Institute
     of Applied Chemistry, Chinese Academy of Sciences, Changchun, 130022,
     Peop. Rep. China
SO
     Fenxi Huaxue (2007), 35(5), 677-680
     CODEN: FHHHDT; ISSN: 0253-3820
PB
     Kexue Chubanshe
DT
     Journal
LΑ
     Chinese
L7
     ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
ΤI
     Analysis of complex gene expression profiles using an analysis of the
     cellular composition of the sample to identify cell-type-specific
     signatures
     A method of identifying cell type-specific gene expression profile
AB
     signatures in a biol. sample is described. The method involves determining the
     gene expression profile of the sample using a defined set of informative
     genes. The cellular composition of the sample is the analyzed to allow the
     contributions from individual cell types to be subtracted from the
     complete profile. The information can be used to model expression
     profiles and differences between predicted and observed profiles may be
     predictively useful, e.g. in the diagnosis or prognosis of disease.
AN
     DN
     143:380829
TI
     Analysis of complex gene expression profiles using an analysis of the
     cellular composition of the sample to identify cell-type-specific
IN
     Haeupl, Thomas; Gruen, Joachim; Radbruch, Andreas; Burmester,
     Gerd-Ruediger; Kaps, Christian; Gruetzkau, Andreas
PA
     Oligene GmbH, Germany
     PCT Int. Appl., 83 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     German
FAN.CNT 1
     PATENT NO.
                         KIND
                                 DATE
                                            APPLICATION NO.
                                                                     DATE
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                                 _____
                                             _____
PI
     WO 2005095644
                          A2
                                 20051013
                                             WO 2005-EP3520
                                                                     20050404
     WO 2005095644
                                 20060413
                          A3
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
             SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
             ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     DE 102004016437
                          A1
                                 20051020
                                             DE 2004-102004016437
                                                                     20040404
     EP 1733050
                          A2
                                 20061220
                                           EP 2005-716523
                                                                     20050404
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             IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRAI DE 2004-102004016437 A
                                 20040404
     WO 2005-EP3520
                         W
                                 20050404
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ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
L7
TI
     Means and methods for detecting endoglycosidase activity
     The invention provides a method for detecting an activity of an
AB
     endoglycosidase comprising providing said endoglycosidase with a substrate
     of said endoglycosidase and detecting cleavage of said substrate, further
     comprising at least partly inhibiting the transglycosidase activity of
     said endoglycosidase. Said transglycosidase activity is preferably
     inhibited by chemical modifying said substrate such that transglycosylation
     of said substrate by said endoglycosidase is at least partly inhibited
     while said endoglycosidase is still capable of cleaving said substrate.
     In one embodiment said substrate comprises an oligosaccharide chain. The
     invention enables improved tests for detecting activities of
     endoglycosidases which are involved in a wide range of important (patho)
     biol. processes, such as lysosomal storage disease, chronic inflammation,
     sepsis, thalassemia, and bladder cancer. Compds. and kits
     suitable for use in a method of the invention are also provided.
     Furthermore methods involving competitive inhibitors are disclosed as well
     as methods for the synthesis of glycosylated substrates involving the
     transglycosidase activity of endoglycosidase.
AN
     2003:892942 HCAPLUS <<LOGINID::20070614>>
DN
     139:361245
ΤI
     Means and methods for detecting endoglycosidase activity
IN
     Aerts, Johannes Maria Franciscus Gerardus
PΑ
     Academisch Ziekenhuis Bij de Universiteit van Amsterdam, Neth.
so
     PCT Int. Appl., 77 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 2
     PATENT NO.
                       KIND DATE
                                        APPLICATION NO.
                       ----
     WO 2003093497
     ------
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                                20031113 WO 2003-NL316
PΙ
                         A1
                                                                  20030429
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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     EP 1359227
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                         A1
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     AU 2003228137
                                20031117
                                           AU 2003-228137
                         A1
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     EP 1499743
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     EP 1499743
                         В1
                                20070606
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                                           US 2004-977509
     US 2005158814
                         A1
                                20050721
                                                                   20041029
PRAI EP 2002-76854
                          Α
                                20020429
     US 2002-376107P
                         Ρ
                                20020429
     WO 2003-NL316
                         W
                                20030429
RE.CNT 4
              THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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- L7 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Chemical and biological characteristics of human lysozyme isolated from placenta
- AB Lysozyme (I) was isolated from human placenta by complex formation with chitin. The mol. weight was estimated as 15,000 by gel filtration on Sephadex G-75. The amino acid composition resembled that of hen egg white I, but with less serine and cystine and more glutamic acid.

Antibacterial effects of I on mice having staphylococcal and coli sepsis were investigated. In the case of staphylococcal sepsis, optimal results were observed when I was administered i.m. either simultaneously with or 2 hr after the infection. Administration of I after 4 hr failed to produce any curative effect. In the case of coli sepsis, I was most active when administered simultaneously with the infection.

- AN 1973:463007 HCAPLUS <<LOGINID::20070614>>
- DN 79:63007
- TI Chemical and biological characteristics of human lysozyme isolated from placenta
- AU Pokidova, N. V.; Zhuravleva, T. P.; Babayan, S. S.; Ermol'eva, Z. V.
- CS Dep. Microbiol., Cent. Postgrad. Train. Inst., Moscow, USSR
- SO Advan. Antimicrob. Antineoplastic Chemother., Proc. Int. Congr. Chemother., 7th (1972), Meeting Date 1971, Volume 1, Issue Pt. 2, 1089-90. Editor(s): Hejzlar, Miroslav. Publisher: Univ. Park Press, Baltimore, Md. CODEN: 26QZAP
- DT Conference
- LA English

=> d his

(FILE 'HOME' ENTERED AT 13:22:26 ON 14 JUN 2007)

FILE 'HCAPLUS' ENTERED AT 13:25:03 ON 14 JUN 2007

- L1 30329 S LYSOZYME OR MURAMIDASE
- L2 21350 S SIRS OR (SYSTEMIC INFLAMMATORY RESPONSE) OR SEPSIS OR ((SEPTI
- L3 1362 S (MYOCARDIAL(W) (DYSFUNCTION OR DEPRESSION))
- L4 49845 S (CHITOBIOSE OR CHITOTRIOSE OR CHITIN OR CHITOSAN OR (N-ACETYL
- L5 57 S L1 AND L2
- L6 4 S L1 AND L2 AND L3
- L7 6 S L1 AND L2 AND L4
- L8 2 S L1 AND L2 AND L3 AND L4

FILE 'STNGUIDE' ENTERED AT 13:25:11 ON 14 JUN 2007

FILE 'HCAPLUS' ENTERED AT 13:26:02 ON 14 JUN 2007

FILE 'STNGUIDE' ENTERED AT 13:26:03 ON 14 JUN 2007

FILE 'HCAPLUS' ENTERED AT 13:26:20 ON 14 JUN 2007

FILE 'STNGUIDE' ENTERED AT 13:26:20 ON 14 JUN 2007

FILE 'HCAPLUS' ENTERED AT 13:26:57 ON 14 JUN 2007

FILE 'STNGUIDE' ENTERED AT 13:26:57 ON 14 JUN 2007

=> log hold

COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.06 36.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

CA SUBSCRIBER PRICE ENTRY SESSION 0.00 -6.24

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:27:05 ON 14 JUN 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: SSPTAEXO1623

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * * SESSION RESUMED IN FILE 'STNGUIDE' AT 13:45:33 ON 14 JUN 2007 FILE 'STNGUIDE' ENTERED AT 13:45:33 ON 14 JUN 2007 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 0.06	TOTAL SESSION 36.16
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) CA SUBSCRIBER PRICE	SINCE FILE ENTRY 0.00	TOTAL SESSION -6.24
=> file hcaplus COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 0.12	TOTAL SESSION 36.22
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) CA SUBSCRIBER PRICE	SINCE FILE ENTRY 0.00	TOTAL SESSION -6.24

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FILE COVERS 1907 - 14 Jun 2007 VOL 146 ISS 25 FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s (lysozyme or muramidase) (3a) (inhibi?)

29907 LYSOZYME 1204 MURAMIDASE 1937207 INHIBI?

L9 1118 (LYSOZYME OR MURAMIDASE) (3A) (INHIBI?)

=> s 12 and 19

L10 7 L2 AND L9

=> s 110 and (PY<2004 or AY<2004 or PRY<2004)

23932765 PY<2004 4727638 AY<2004

4204018 PRY<2004

L11 5 L10 AND (PY<2004 OR AY<2004 OR PRY<2004)

=> file stnguide

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 2.60 38.82 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -6.24

FILE 'STNGUIDE' ENTERED AT 13:46:58 ON 14 JUN 2007 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jun 8, 2007 (20070608/UP).

=> d l11 1-5 ti abs bib

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

- L11 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of treating inflammation
- AB Methods and compns. for treating myocardial dysfunction or inflammation are described. The methods of the invention involve administering an agent that can inhibit lysozyme to an animal in need thereof. Preferred lysozyme inhibitors include TAC (N,N',N"-triacetylglucosamine, chitotriose) and chitobiose.
- AN 2004:905606 HCAPLUS <<LOGINID::20070614>>
- DN 141:360677
- TI Methods of treating inflammation
- IN Mink, Steven N.; Jacobs, Hans; Bose, Deepak; Duke, Krika; Light, R. Bruce
- PA Can.
- SO U.S. Pat. Appl. Publ., 70 pp. CODEN: USXXCO
- DT Patent
- LA English
- FAN.CNT 1

P.	ATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US	5 2004214792	A1	20041028	US 2004-762581	20040123 <
CZ	A 2428744	A1	20040724	CA 2003-2428744	20030512 <
PRAI US	S 2003-442060P	P	20030124	<	,

- L11 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Inhibitory effect of egg white lysozyme on ceftazidime-induced release of endotoxin from Pseudomonas aeruginosa
- AB The inhibitory effect of egg white lysozyme (LZM) on ceftazidime (CFT)-induced release of endotoxin from Pseudomonas aeruginosa was studied. P. aeruginosa PAO1 was inoculated in nutritional broth or diluted rabbit blood free of antibiotics in the presence or absence of LZM and incubated at 37° on a water bath shaker. $\beta\text{-Lactam}$ antibiotic CFT was added to cultures at 3.5 h or 5 h (diluted rabbit blood culture) after inoculation. After 3 h of CFT treatment, the supernatants from different bacterial cultures were prepared by centrifuge and the concns. of endotoxin in the supernatants were measured. The bacterial supernatants

were also added to a murine macrophage cell line RAW 264.7 or i.v. injected into carrageenin-sensitized mice. Tumor necrosis factor- α $(TNF\alpha)$ and nitric oxide (NO) concns. in RAW 264.7 supernatants or in mouse sera were tested. CFT treatment alone obviously inhibited the growth of P. aeruginosa PAO1 accompanied by strong and rapid bacteriolysis and released relatively high concentration of endotoxin from bacteria both in nutritional broth and in diluted rabbit blood cultures. The bacterial supernatant from CFT treatment alone yielded high concns. of $TNF\alpha$ both in RAW 264.7 cells and in mice and high level of NO in RAW 264.7 cells. Treatment with the combination of LZM and CFT evidently blocked the lysis of bacteria and reduced the release of endotoxin without decreasing bactericidal activity of CFT. TNF α and NO productivity of the supernatants prepared from the LZM/CFT combination treated bacterial cultures were significantly decreased both in RAW 264.7 cells and in mice, indicating that the inflammatory activity was reduced. LZM can effectively prevent CFT-induced bacteriolysis, endotoxin release, and subsequent pro-inflammatory factor production but without decreasing bactericidal activity of CFT, causing the disassocn. of bactericidal activity and bacteriolysis. Thus, LZM might be important for preventing endotoxemia in Gram-neg. sepsis with the treatment of antibiotics.

- AN 2004:791028 HCAPLUS <<LOGINID::20070614>>
- DN 143:3863
- TI Inhibitory effect of egg white lysozyme on ceftazidime-induced release of endotoxin from Pseudomonas aeruginosa
- AU Liang, Aihua; Xue, Baoyun; Liang, Rixin; Wang, Jinhua; Wang, Dan
- CS Institute of Chinese Materia Medica, China Academy of Traditional Chinese Medicine, Beijing, 100700, Peop. Rep. China
- SO Yaoxue Xuebao (2003), 38(11), 801-804 CODEN: YHHPAL; ISSN: 0513-4870
- PB Yaoxue Xuebao Bianjibu
- DT Journal
- LA Chinese
- L11 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of inhibiting protein degradation to combat muscle wasting and methods of screening for such inhibitors
- AB Methods are described for identifying inhibitors of the accelerated ubiquitin conjugation that occurs in disease states involving muscle wasting. Methods are also described for inhibiting the loss of muscle mass in such disease states by the use of inhibitors of key components of the N-end rule pathway for protein ubiquitination. When the levels of the N-end rule ubiquitin conjugating enzymes E214k and E3α were increased in soluble exts. of rabbit muscle, the degradation of endogenous proteins increased. A 2 mM Lys-Ala and Phe-Ala combination inhibited proteolysis.
- AN 1998:385511 HCAPLUS <<LOGINID::20070614>>
- DN 129:49665
- TI Methods of inhibiting protein degradation to combat muscle wasting and methods of screening for such inhibitors
- IN Goldberg, Alfred L.; Bhoite-Solomon, Vered
- PA President and Fellows of Harvard College, USA; Goldberg, Alfred L.; Bhoite-Solomon, Vered
- SO PCT Int. Appl., 76 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

	PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
PΙ	WO 9823283		A1	19980604	WO 1997-US21421	19971125 <
	W: AU,	CA, JP,	US			
	5					

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9854538 A 19980622 AU 1998-54538 19971125 <--

PRAI US 1996-755713 Α 19961125 <--W WO 1997-US21421 19971125 <--THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 5 ALL CITATIONS AVAILABLE IN THE RE FORMAT . L11ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN Pharmaceutical compositions containing lysozyme dimer as tumor necrosis TT factor inhibitors Pharmaceutical compns. containing dimerized form of lysozyme (I) are used for AB inhibiting biosynthesis of tumor necrosis factor (TNF) in animals and humans. An injection of 2mg I in 10 mL phosphate buffered saline to calves suffering from gastroenteritis and bronchopneumonia cured ≥90 and ≥85% of the disease resp., and decreased TNF level in blood. AN DN 120:144184 TI Pharmaceutical compositions containing lysozyme dimer as tumor necrosis factor inhibitors IN Kiczka, Witold PA Nika Health Products Ltd., Liechtenstein; Rosenich, Paul SO PCT Int. Appl., 37 pp. CODEN: PIXXD2 DT Patent English LAFAN.CNT 4 KIND DATE APPLICATION NO. PATENT NO. ____ WO 1993-EP1841 PΙ WO 9401127 . A1 19940120 19930713 <--W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG PL 173978 B1 19980529 PL 1992-295273 19920713 <--AU 9345686 19940131 AU 1993-45686 Α 19930713 <--AU 677786 B2 19970508 ZA 9305046 19940207 ZA 1993-5046 19930713 <--A CN 1993-116771 CN 1087278 Α 19940601 19930713 <--CN 1057937 В 20001101 EP 651654 EP 1993-915903 Α1 19950510 19930713 <--EP 651654 В1 20031022 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE JP 07508744 T 19950928 JP 1994-502985 19930713 <--HU 70973 A2 19951128 HU 1995-98 19930713 <--HU 218151 В. 20000628 RO 112580 B1 19971128 RO 1995-41 19930713 <--BR 9306722 Α 19981208 BR 1993-6722 19930713 <--PL 176407 В1 19990531 PL 1993-307244 19930713 <--RU 2145875 C1 20000227 RU 1995-105517 19930713 <--CZ 286725 В6 20000614 CZ 1995-85 19930713 <--SK 282377 В6 20020107 SK 1995-40 19930713 <--AT 252392 Т 20031115 AT 1993-915903 19930713 <--PT 651654 Т PT 1993-915903 20040331 19930713 <--Т3 ES 2074037 20040701 ES 1993-915903 19930713 <--BG 63331 В1 20011031 BG 1994-99287 19941222 <--NO 9500076 Α 19950111 NO 1995-76 19950109 <--FI 9500144 Α 19950112 FI 1995-144 19950112 <--US 6132715 ·A 20001017 US 1995-476561 19950607 <--NZ 299377 NZ 1996-299377 Α 20010223 19960913 <--

PRAI PL 1992-295273

US 1992-865002

WO 1993-EP1841

US 1995-351375

Α

A2

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B3

19920713

19920408

19930713

19950213

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ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
     Inhibition of some human neutrophil functions by the cyclooxygenase
     inhibitor ketorolac tromethamine
     Ketorolac tromethamine, a new nonsteroidal anti-inflammatory agent of the
AB
     pyrrolo-pyrrole group, was assayed for inhibitory effects on
     polymorphonuclear leukocytes (PMN) in a variety of systems. Ketorolac
     inhibited PMN superoxide anion generation, lysozyme release,
     myeloperoxidase release, adherence to plastic surfaces, and chemotaxis in
     response to N-formyl-methionyl-leucyl-phenylalanine (fMLP) in a
     dose-dependent manner. Ketorolac also inhibited phorbol myristate
     acetate-stimulated adherence of PMN to bovine pulmonary artery endothelial
     cells. The drug inhibited lysozyme and
     myeloperoxidase release by PMN in response to C5a but failed to inhibit
     C5a stimulation of PMN in any of the other assays. Levels of ketorolac
     required to inhibit PMN function in most systems were in the range of 0.2
     to 1.0 mg/mL, but chemotaxis to fMLP was inhibited by concns. of ketorolac
     as low as 1 µg/mL. Ketorolac, currently the only nonsteroidal
     anti-inflammatory drug available in a parenteral form may have therapeutic
     usefulness in a variety of conditions thought to be mediated in part by
     PMN, including sepsis.
     1992:503820 HCAPLUS <<LOGINID::20070614>>
AN
DN
     117:103820
ΤI
     Inhibition of some human neutrophil functions by the cyclooxygenase
     inhibitor ketorolac tromethamine
ΑU
     Hyers, Thomas M.; Tricomi, Sally M.; Liao, Jeng Jong
     Sch. Med., St. Louis Univ., St. Louis, MO, 63110-0250, USA
CS
     Journal of Leukocyte Biology (1992), 51(5), 490-5
so
     CODEN: JLBIE7; ISSN: 0741-5400
DТ
     Journal
LA
     English
=> d his
     (FILE 'HOME' ENTERED AT 13:22:26 ON 14 JUN 2007)
     FILE 'HCAPLUS' ENTERED AT 13:25:03 ON 14 JUN 2007
          30329 S LYSOZYME OR MURAMIDASE
L1
          21350 S SIRS OR (SYSTEMIC INFLAMMATORY RESPONSE) OR SEPSIS OR ((SEPTI
L2
L3
           1362 S (MYOCARDIAL (W) (DYSFUNCTION OR DEPRESSION))
          49845 S (CHITOBIOSE OR CHITOTRIOSE OR CHITIN OR CHITOSAN OR (N-ACETYL
L4
             57 S L1 AND L2
L5
              4 S L1 AND L2 AND L3
L6
L7
              6 S L1 AND L2 AND L4
                S L1 AND L2 AND L3 AND L4
L8
     FILE 'STNGUIDE' ENTERED AT 13:25:11 ON 14 JUN 2007
     FILE 'HCAPLUS' ENTERED AT 13:26:02 ON 14 JUN 2007
     FILE 'STNGUIDE' ENTERED AT 13:26:03 ON 14 JUN 2007
     FILE 'HCAPLUS' ENTERED AT 13:26:20 ON 14 JUN 2007
     FILE 'STNGUIDE' ENTERED AT 13:26:20 ON 14 JUN 2007
     FILE 'HCAPLUS' ENTERED AT 13:26:57 ON 14 JUN 2007
     FILE 'STNGUIDE' ENTERED AT 13:26:57 ON 14 JUN 2007
     FILE 'HCAPLUS' ENTERED AT 13:46:53 ON 14 JUN 2007
L9
           1118 S (LYSOZYME OR MURAMIDASE) (3A) (INHIBI?)
L10
              7 S L2 AND L9
L11
              5 S L10 AND (PY<2004 OR AY<2004 OR PRY<2004)
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FILE 'STNGUIDE' ENTERED AT 13:46:58 ON 14 JUN 2007

FILE 'HCAPLUS' ENTERED AT 13:47:07 ON 14 JUN 2007

FILE 'STNGUIDE' ENTERED AT 13:47:07 ON 14 JUN 2007

=> log hold

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STN INTERNATIONAL SESSION SUSPENDED AT 13:47:12 ON 14 JUN 2007

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PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * * SESSION RESUMED IN FILE 'STNGUIDE' AT 14:19:59 ON 14 JUN 2007 FILE 'STNGUIDE' ENTERED AT 14:19:59 ON 14 JUN 2007 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	55.69
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-10.14
=> file registry COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY 0.06	SESSION 55.69
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY 0.00	SESSION -10.14

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STRUCTURE FILE UPDATES: 13 JUN 2007 HIGHEST RN 937234-16-7 DICTIONARY FILE UPDATES: 13 JUN 2007 HIGHEST RN 937234-16-7

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http://www.cas.org/support/stngen/stndoc/properties.html

=> s ketorolac/cn

L12 1 KETOROLAC/CN

=> d 11

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y) /N:n

=> d 112

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN

RN 74103-06-3 REGISTRY

ED Entered STN: 16 Nov 1984

CN 1H-Pyrrolizine-1-carboxylic acid, 5-benzoyl-2,3-dihydro- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Pyrrolizine-1-carboxylic acid, 5-benzoyl-2,3-dihydro-, (\pm) -

OTHER NAMES:

CN (±)-Ketorolac

CN Ketorolac

CN RS 37619

DR 66635-83-4

MF C15 'H13 N O3

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS,

RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL (*File contains numerically searchable property data)

Other Sources: WHO

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1015 REFERENCES IN FILE CA (1907 TO DATE)

37 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1020 REFERENCES IN FILE CAPLUS (1907 TO DATE)

'CPALUS' IS NOT A VALID FILE NAME

SESSION CONTINUES IN FILE 'REGISTRY'

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=> file caplus

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FULL ESTIMATED COST 7.35 63.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

CA SUBSCRIBER PRICE ENTRY SESSION 0.00 -10.14

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FILE COVERS 1907 - 14 Jun 2007 VOL 146 ISS 25 FILE LAST UPDATED: 13 Jun 2007 (20070613/ED)

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=> s l12/thu and l2 COMMAND INTERRUPTED

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=> s (l12/thu) and l2 COMMAND INTERRUPTED

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=> s l12/thu

1020 L12

900551 THU/RL

L13 773 L12/THU

(L12 (L) THU/RL)

=> s 113 and 12

890 SIRS

103641 SYSTEMIC

180565 INFLAMMATORY

1596202 RESPONSE

1915 SYSTEMIC INFLAMMATORY RESPONSE

(SYSTEMIC (W) INFLAMMATORY (W) RESPONSE)

15541 SEPSIS

13609 SEPTIC

254096 TOXIC

146275 SHOCK

6500 (SEPTIC OR TOXIC) (W) SHOCK

7 L13 AND L2

=> d l14 1-7 ti

L14

- L14 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Monocyte chemotactic protein 1-immunoglobulin fusions for targeting and treating CCR2-mediated inflammation
- L14 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Compositions comprising β -blockers and methods for ameliorating cachexia
- L14 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Use of Oxcarbazepine to Treat a Pediatric Patient With Resistant Complex Regional Pain Syndrome
- L14 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of amides of pyrazolamines and anilines as well as analogs as cytokine inhibitors for the treatment of inflammatory diseases
- L14 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of 3-(pyrimidin-4-yl)-6,7-dihydro-5H-pyrazolo[1,2-a]pyrazol-1-ones which provide analgesia
- L14 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of anilinopyrimidines as IKK inhibitors
- L14 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of anilinopyrimidines as JNK pathway inhibitors

=> d l14 2 4 5 6 7 ti abs bib

- L14 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Compositions comprising β -blockers and methods for ameliorating cachexia
- AB The invention provides prepns., formulations, kits and other products of manufacture (e.g., blister packs) comprising combinations of beneficial ingredients that are serviceable as therapies for improving states and disease symptoms such as involving inflammation, excessive sympathoneural drive, cachexia, anorexia, and anorexia-cachexia, as well as stress or anxiety related thereto, and methods of making and using them. The invention provides compns. and therapies comprising use of a β -adrenergic antagonist (β -blockers, e.g., propranolol) in combination with an anti-inflammatory agent, e.g., a nonsteroidal anti-inflammatory drug (NSAID), an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin receptor blocker (ARB), an anabolic steroid, a natural oil or fatty acid or any combination thereof. The therapeutic combination or pharmaceutical composition is formulated or manufactured as feed, a

food, a liquid, an elixir, an aerosol, a spray, a powder, a tablet, a pill, a capsule, a gel, a geltab, a nanosuspension, a nanoparticle a microgel or a suppository. Thus, a treatment protocol for subjects with non-hematol. metastatic cancer was proposed comprising a combination of β -blocker atenolol (Tenormin) 12.5 to 100 mg per day and NSAID etodolac (Lodine). Since the effect of atenolol and etodolac are opposite on blood pressure, it is important that patient compliance be maintained for safety. Dose was increased to obtain a heart rate of approx. 60 bpm with blood pressure

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maintained above 90/60.
```

AN

DN 145:383494

Compositions comprising β -blockers and methods for ameliorating TI cachexia

IN Bascomb, Newell; Maki, John; Young, Fredric

PA Vicus Therapeutics Spe 1, LLC, USA

SO PCT Int. Appl., 136pp.

CODEN: PIXXD2

DTPatent

English LA

FAN.CNT 1																			
	PA:	rent 1	NO.			KIND		DATE		APPLICATION NO.						DATE			
							-												
ΡI	WO	2006102476			A2 20060928			1	WO 2	006-1		20060321							
	WO	2006102476			A3 2007042			0426											
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			CN,	CO,	CR,	CU,	CZ,	DΕ,	DK,	DM,	DΖ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,	
		•	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KN,	KP,	KR,	
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			ΜZ,	NA,	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	ΡL,	PT,	RO,	RU,	SC,	SD,	SE,	
			SG,	SK,	SL,	SM,	SY,	ΤĴ,	TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UΖ,	VC,	
			VN,	YU,	ZA,	ZM,	zw												
		RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	
			IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	
			CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,	
			GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	AM,	ΑZ,	BY,	
			KG,	ΚZ,	MD,	RU,	ΤJ,	TM,	ΑP,	EA,	EP,	OA							
PRAI	US	2005	-6642	225P		P		2005	0321										
	US	2005	-713	526P		P		2005	0831										
	US	2005	-7354	432P		P		2005	1110										
	US	2005	-753	436P		P		2005	1222										

L14 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

Preparation of amides of pyrazolamines and anilines as well as analogs as ΤI cytokine inhibitors for the treatment of inflammatory diseases

GI

Title compds., such as I and II (four Markush structures are claimed), AΒ wherein X = C(0), C(S) or CH2; G = (un) substituted carbocyclyl or heterocyclyl; Ar = indazolyl, indolyl, pyrazolyl, alkyl, etc.; L = covalent bond or (un) substituted carbon chain; Q = H, (un) substituted amino, cycloalkyl, heterocyclyl, alkoxy or sulfonyl; with some limitations and exclusions, and stereoisomers, tautomers, solvates, prodrugs and pharmaceutically acceptable salts thereof, were prepared as cytokine

inhibitors. For instance, cyclization of p-tolylhydrazine hydrochloride with 4,4-dimethyl-3-oxopentanenitrile to the corresponding pyrazolamine (92% yield) followed by EDC-mediated coupling with indazole-3-carboxylic acid gave indazolopyrazole III (40% yield). I were found to have activity in the TNFa ELISA assay, with some compds. having IC50 < 10 μM . Therefore, I and their pharmaceutical compns. are useful in preventing or treating conditions mediated by cytokines, such as arthritis and inflammatory diseases.

- AN 2005:238947 CAPLUS <<LOGINID::20070614>>
- DN 142:316831
- TI Preparation of amides of pyrazolamines and anilines as well as analogs as cytokine inhibitors for the treatment of inflammatory diseases
- IN Boman, Erik; Ceide, Susana C.; Dahl, Russell; Delaet, Nancy G. J.; Ernst, Justin; Montalban, Antonio G.; Kahl, Jeffrey D.; Larson, Christopher; Miller, Stephen; Nakanishi, Hiroshi; Roberts, Edward; Saiah, Eddine; Sullivan, Robert; Wang, Zhijun
- PA Kemia, Inc., USA
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- L14 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of 3-(pyrimidin-4-yl)-6,7-dihydro-5H-pyrazolo[1,2-a]pyrazol-1-ones which provide analgesia

Ι

AB The present invention relates to compds. which are capable of preventing the extracellular release of inflammatory cytokines, said compds., including all enantiomeric and diastereomeric forms and pharmaceutically acceptable salts thereof, have the formula (I) [R = O(CH2)kR3], (un) substituted NH2 (wherein k = 0.5; R3 = (un) substituted alkyl, hydrocarbyl, heterocyclyl, aryl, alkylenearyl, heteroaryl, or alkyleneheteroaryl); R1 = (un)substituted (hetero)aryl; R2 = H, (CH2)jO(CH2)nR8, (CH2)jNR9aR9b, (CH2)jCO2R10, (CH2)jOCO2R10, (CH2) jCON(R10)2, (CH2) jOCON(R10)2; or two R2 units can be taken together to form a CO unit (wherein R8, R9a, R9b, R10 = H, alkyl; or R9a and R9b are taken together to form carbocyclic or heterocyclic ring; j, n = 0-5); Z = O, S, NR11, NOR11 (R11 = H, alkyl)]. Interleukin-1 (IL-1) and tumornecrosis factor- α (TNF- α) are among the important biol. substances known collectively as cytokines and understood to mediate the inflammatory response associated with the immunol. recognition of infectious agents. These pro-inflammatory cytokines are suggested as an important mediators in many disease states or syndromes, inter alia, rheumatoid arthritis, osteoarthritis, inflammatory bowel disease (IBS), septic shock, cardiopulmonary dysfunction, acute respiratory disease, cachexia, and therefore responsible for the progression and manifestation of human disease states. The compds. I can provide pain relief, and reduce psoriasis in humans or higher mammal (data provided for one of the compds. I). Thus, 6.0 q Me 4-fluorophenylacetate was added to a cold (-78°) solution of lithium diisopropylamide (2M, 21.4 mL)in THF and stirred at -78° for 1 h at -78°, followed by adding dropwise a solution of 6.0 g 2-methylsulfanylpyrimidine-4carboxaldehyde (preparation given) in 30 mL THF and the resulting mixture was stirred for 45 min at -78° to give, after workup and silica gel chromatog., 8.7 g 2-(4-fluorophenyl)-3-(2-methylsulfanylpyrimidin-4-yl)-3hydroxypropionic acid Me ester (II) (76 %). To a suspension of CrO3 in CH2Cl2 (300 mL) was added pyridine and stirred vigorously for 1 h at room temperature, followed by adding a solution of the crude II prepared above in 50 mL

CH2Cl2 dropwise, and the reaction mixture was stirred at room temperature for 16 h

to give, after workup and silica gel chromatog., 3.7 g
2-(4-fluorophenyl)-3-(2-methylsulfanylpyrimidin-4-yl)-3-oxopropionic acid
Me ester (III) (43% yield) as a yellow solid. To a solution of 7.8 g
pyrazolidine in 100 mL pyridine was added 11.5 g 2-(4-fluorophenyl)-3-(2methylsulfanylpyrimidin-4-yl)-3-oxopropionic acid Me ester and heated to
90° for 16 h to give, after silica gel chromatog., 3.9 g
2-(4-fluorophenyl)-3-(2-methylsulfanylpyrimidin-4-yl)-6,7-dihydro-5Hpyrazolo[1,2-a]pyrazol-1-one (37%) which (1.3 g) was dissolved in a 1:1
mixture of THF and MeOH (56 mL), treated dropwise with 9.34 g Oxone in 42 mL
H2O, and stirred at room temperature for 1 h to give 2-(4-fluorophenyl)-3-(2methanesulfonylpyrimidin-4-yl)-6,7-dihydro-5H-pyrazolo[1,2-a]pyrazol-1one. The pharmaceutical compns. comprising the compound I are claimed.

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RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN Preparation of anilinopyrimidines as IKK inhibitors TI GI

The title compds. [I; R1 = (un) substituted (hetero) aryl; R2 = H; R3 = H, AΒ alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9,

etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of IKK, particularly IKK-2, were prepared E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of \leq 1 μ M in the IKK-2 enzyme assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to IKK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds. 137:33310 Preparation of anilinopyrimidines as IKK inhibitors Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E. Signal Pharmaceuticals, Inc., USA PCT Int. Appl., 194 pp. CODEN: PIXXD2 Patent English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ______ _ - - -----------_____ WO 2002046171 **A2** 20020613 WO 2001-US46403 20011205 WO 2002046171 **A**3 20030123 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2003203926 A1 20031030 US 2001-4642 20011204 US 7122544 B2 20061017 CA 2431160 Α1 20020613 CA 2001-2431160 20011205 AU 2002020195 AU 2002-20195 Α5 20020618 20011205

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AB The title compds. [I; R1 = (un) substituted (hetero) aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9,

etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of the JNK pathway, were prepared E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of \leq 10 μM in the JNK2 assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to inhibition of the JNK pathway. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds. 2002:449661 CAPLUS <<LOGINID::20070614>> 137:33309 Preparation of anilinopyrimidines as JNK pathway inhibitors Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E. Signal Pharmaceuticals, Inc., USA PCT Int. Appl., 199 pp. CODEN: PIXXD2 Patent English FAN.CNT 2 PATENT NO. APPLICATION NO. KIND DATE DATE ---------------_ _ _ _ _ _ _ _ _ _ _ _ WO 2002046170 20020613 WO 2001-US46402 A2 20011205 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG CA 2430966 20020613 CA 2001-2430966 Α1 20011205 AU 2002027214 20020618 AU 2002-27214 **A5** 20011205 EP 1349840 20031008 EP 2001-996103 A2 20011205 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR JP 2004534728 Т 20041118 JP 2002-547909 20011205

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